

PRELIMINARY AMENDMENT

Serial Number: Unknown

Filing Date: June 12, 2000

Title: HIGH DOSE RADIONUCLIDE COMPLEXES FOR BONE MARROW SUPPRESSION

Page 2

Dkt: 295.044US1

86. A therapeutic method for treating a bone-associated cancer comprising:
- (a) hydrating said cancer patient by administration of water;
  - (b) parenterally administering a single dose of  $^{166}\text{Ho}$ -DOTMP to said patient in an aqueous vehicle comprising an effective antiradiolytic amount of a pharmaceutically acceptable radioprotectant, said dose being effective to deliver about 20-60 Gy to the bone marrow of said patient;
  - (c) administering a dose of at least about 200 mg/m<sup>2</sup> melphalan to the patient; and
  - (d) providing the patient with an autologous stem cell transplant;

wherein the patient is not subjected to total body irradiation in conjunction with the therapeutic method.

87. The method of claim 86 wherein the cancer is multiple myeloma.

88. The method of claim 86 wherein the cancer is metastatic breast or prostate cancer.

89. The method of claim 86 wherein the cancer is Ewing's sarcoma.

90. The method of claim 86, 87 or 88 wherein the radioprotectant is ascorbic acid or gentisic acid.

91. The method of claim 90 wherein the concentration of ascorbic acid is about 35-75 mg/ml.

92. The method of claim 91 wherein the vehicle is buffered to about pH 7-8.

93. The method of claim 90, 91 or 92 wherein the dose is effective to deliver about 20-30 Gy to the bone marrow of said patient.

**PRELIMINARY AMENDMENT**

Serial Number: Unknown

Filing Date: June 12, 2000

Title: HIGH DOSE RADIONUCLIDE COMPLEXES FOR BONE MARROW SUPPRESSION

Page 3

Dkt: 295.044US1

94. A method to prepare a medicament for the treatment of bone-associated cancer comprising combining  $^{166}\text{Ho}$ -DOTMP in an aqueous vehicle with an effective antiradiolytic amount of a pharmaceutically acceptable radioprotectant, wherein said medicament is effective to deliver a dose of about 20-60 Gy to the bone marrow of said patient in a single infused dose.
95. The use of claim 94 wherein the radioprotectant is ascorbic acid or gentisic acid.
96. The method of claim 94 or 95 wherein the vehicle is buffered to about pH 7-8.
97. The method of claim 94 wherein the cancer is multiple myeloma.
98. The method of claim 94 wherein the cancer is Ewing's sarcoma.
99. The method of claim 94 wherein the cancer is metastatic breast or prostate cancer.
100. A liquid pharmaceutical composition comprising  $^{166}\text{Ho}$  complexed with 1,4,7,10-tetraazacyclododecanetetramethylene-phosphonic acid (DOTMP) and an effective antiradiolytic amount of a pharmaceutically acceptable radioprotectant.
101. The composition of claim 100, wherein the radioprotectant is ascorbic acid or gentisic acid.
102. The composition of claim 101 comprising about 35-75 mg ascorbic acid/ml of composition.
103. The composition of claim 100 or 101 wherein the ratio of DOTMP to  $^{166}\text{Ho}$  is above 3.
104. The composition of claim 100, comprising an aqueous carrier adjusted to pH 7-8.